nanoparticle-encapsulated Taxol for drug delivery in cancer therapy

- AU Sharma, Dayanand; Chelvi, Tamiz P.; Kaur, Jatinder; Chakravorty, Ketaki; De, Tapas K.; Maitra, Amarnath; Ralhan, Ranju
- CS Department of Biochemistry, All India Institute of Medical Sciences, New Delhi, 110029, India
- SO Queology Research (1996), 8 (7/8), 281-286 CODEN: ONREE8; ISSN: 0965-0407
- PB Elsevier
- DT Journal
- LA English
- AB Taxol is a novel antitumor alkaloid that has shown clin. activity against several tumors. However, due to its low aqueous solubility, Cremophor EL (polyoxyethylated castor oil) and ethanol are used as excipients in the pharmaceutical drug formulations. These agents are implicated in hypersensitivity reactions. Hence the goal of this work was to design a novel Taxol formulation using polymeric nanoparticles to eliminate the Cremophor EL vehicle for drug delivery. Polyvinylpyrrolidone nanoparticles containing Taxol were prepared by a reverse microemulsion method. The size of the nanoparticles as determined by quasielastic light scattering was found to be between 50 and 60 nm. The antitumor effect of Taxol encapsulated nanoparticles was evaluated in B16F10 murine melanoma transplanted in C57B1/6 mice. The in vivo efficacy of Taxol-containing nanoparticles as measured by reduction in tumor volume and increased survival time was significantly greater than that of an equivalent concentration of free Taxol. These results suggest that encapsulation of Taxol in polymeric nanoparticles could be useful in improving its therapeutic efficacy in treatment of solid tumors.

### => file uspat

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# => d his

(FILE 'HOME' ENTERED AT 15:15:55 ON 08 AUG 2007)

FILE 'CAPLUS' ENTERED AT 15:16:04 ON 08 AUG 2007

L1 346 S NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL)

L2 83 S L1/TI

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=> s 12
          1300 NANOPAR?/TI
           154 TAXANE/TI
           181 TAXANES/TI
           328 TAXANE/TI
                  ((TAXANE OR TAXANES)/TI)
           156 PACLITAXEL/TI
            10 PACLITAXELS/TI
           166 PACLITAXEL/TI
                  ((PACLITAXEL OR PACLITAXELS)/TI)
            31 DOCETAXEL/TI
           163 TAXOL/TI
             9 TAXOLS/TI
           172 TAXOL/TI
                  ((TAXOL OR TAXOLS)/TI)
             5 (NANOPAR?/TI AND (TAXANE/TI OR PACLITAXEL/TI OR DOCETAXEL/TI OR
L3
               TAXOL/TI))
=> d 1-5 ti
     ANSWER 1 OF 5 USPATFULL on STN
L_3
       Nanoparticulate formulations of docetaxel and
ΤI
       analogues thereof
L3
     ANSWER 2 OF 5 USPATFULL on STN
TI
       Process for producing nanoparticles of paclitaxel
       and albumin
L3
     ANSWER 3 OF 5 USPATFULL on STN
ΤI
       Process for producing nanoparticles of paclitaxel
       and albumin
L3
     ANSWER 4 OF 5 USPATFULL on STN
TI
       Formulations of paclitaxel, its derivatives or its analogs
       entrapped into nanoparticles of polymeric micelles, process
       for preparing same and the use thereof
     ANSWER 5 OF 5 USPATFULL on STN
L3
TI
       Formulations of paclitaxel, its derivatives or its analogs
       entrapped into nanoparticles of polymeric micelles, process
       for preparing same and the use thereof
=> d 5 bib, ab
     ANSWER 5 OF 5 USPATFULL on STN
1.3
       2001:214686 USPATFULL
ΑN
       Formulations of paclitaxel, its derivatives or its analogs
TT
       entrapped into nanoparticles of polymeric micelles, process
       for preparing same and the use thereof
IN
       Maitra, Amarnath, Delhi, India
       Sahoo, Sanjeeb Kumar, Delhi, India
       Ghosh, Prasanta Kumar, New Delhi, India
       Burman, Anand C., Ghaziabad, India
       Mukherjee, Rama, Ghaziabad, India
       Khattar, Dhiraj, Ghaziabad, India
       Kumar, Mukesh, Ghaziabad, India
       Paul, Soumendu, Ghaziabad, India
PA
       Dabur Research Foundation, India (non-U.S. corporation)
       Delhi University, India (non-U.S. corporation)
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B1 20011127

ΡI

US 6322817

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US 1999-401927
                                19990923 (9)
AΙ
       IN 1999-26399
                            19990217
PRAI
DT
       Utility
FS
       GRANTED
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Fubara, Blessing
LREP
       Ladas & Parry
CLMN
       Number of Claims: 32
ECL
       Exemplary Claim: 1
DRWN
       4 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 586
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention relates to pharmaceutical formulations of paclitaxel, its
AB
       derivatives or analogs entrapped into nanoparticles of co-polymeric
       micelles, a process for preparing the same and the use thereof.
=> s 12/ab
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a
field code. You can only add a field code to a term that has no field
code appended to it.
=> d his
     (FILE 'HOME' ENTERED AT 15:15:55 ON 08 AUG 2007)
     FILE 'CAPLUS' ENTERED AT 15:16:04 ON 08 AUG 2007
            346 S NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL)
L1
L_2
             83 S L1/TI
     FILE 'USPATFULL' ENTERED AT 15:19:21 ON 08 AUG 2007
              5 S L2
L3
=> s NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL)
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          2201 TAXANE
          3046 TAXANES
          4022 TAXANE
                  (TAXANE OR TAXANES)
         10624 PACLITAXEL
           163 PACLITAXELS
         10626 PACLITAXEL
                  (PACLITAXEL OR PACLITAXELS)
          4599 DOCETAXEL
            31 DOCETAXELS
          4601 DOCETAXEL
                  (DOCETAXEL OR DOCETAXELS)
         12623 TAXOL
           366 TAXOLS
         12700 TAXOL
                  (TAXOL OR TAXOLS)
L4
          2528 NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL)
=> s 14/ab
          2431 NANOPAR?/AB
           273 TAXANE/AB
           185 TAXANES/AB
           409 TAXANE/AB
                 ((TAXANE OR TAXANES)/AB)
           370 PACLITAXEL/AB
            96 DOCETAXEL/AB
           335 TAXOL/AB
            15 TAXOLS/AB
           342 TAXOL/AB
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# ((TAXOL OR TAXOLS)/AB)

.26 (NANOPAR?/AB AND (TAXANE/AB OR PACLITAXEL/AB OR DOCETAXEL/AB OR TAXOL/AB))

### => d 1-26 ti

L5

- L5 ANSWER 1 OF 26 USPATFULL on STN
- TI Combinations and modes of administration of therapeutic agents and combination therapy
- L5 ANSWER 2 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 3 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 4 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 5 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 6 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 7 OF 26 USPATFULL On STN
- TI Methods and compositions for treating proliferative diseases
- L5 ANSWER 8 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 9 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 10 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 11 OF 26 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L5 ANSWER 12 OF 26 USPATFULL on STN
- TI Compositions and methods for preparation of poorly water soluble drugs with increased stability
- L5 ANSWER 13 OF 26 USPATFULL on STN
- TI Paclitaxel-based antitumor formulation
- L5 ANSWER 14 OF 26 USPATFULL on STN
- TI Combinations and modes of administration of therapeutic agents and combination therapy
- L5 ANSWER 15 OF 26 USPATFULL on STN
- TI Nanoparticulate delivery systems for treating multi-drug resistance
- L5 ANSWER 16 OF 26 USPATFULL on STN

Nanoparticulate formulations of docetaxel and analogues thereof ΤI ANSWER 17 OF 26 USPATFULL on STN L5 TI Process for producing nanoparticles of paclitaxel and albumin L5 ANSWER 18 OF 26 USPATFULL on STN ΤI Tumor targeting drug-loaded particles ANSWER 19 OF 26 USPATFULL on STN L5Water soluble chitosan nanoparticle for delivering an anticancer agent TI and preparing method thereof ANSWER 20 OF 26 USPATFULL on STN L5 ΤI Protein stabilized pharmacologically active agents, methods for the preparation thereof and methods for the use thereof L5 ANSWER 21 OF 26 USPATFULL on STN ΤI Paclitaxel-based antitumor formulation ANSWER 22 OF 26 USPATFULL on STN L5 ΤI Process for producing nanoparticles of paclitaxel and albumin ANSWER 23 OF 26 USPATFULL on STN 1.5 Compositions and methods for administration of pharmacologically active ΤI compounds ANSWER 24 OF 26 USPATFULL on STN  $L_5$ Formulations of paclitaxel, its derivatives or its analogs entrapped TI into nanoparticles of polymeric micelles, process for preparing same and the use thereof ANSWER 25 OF 26 USPATFULL on STN L5 Formulations of paclitaxel, its derivatives or its analogs entrapped TI into nanoparticles of polymeric micelles, process for preparing same and the use thereof ANSWER 26 OF 26 USPATFULL on STN L5 Protein stabilized pharmacologically active agents, methods for the TI preparation thereof and methods for the use thereof => d his (FILE 'HOME' ENTERED AT 15:15:55 ON 08 AUG 2007) FILE 'CAPLUS' ENTERED AT 15:16:04 ON 08 AUG 2007 L1 346 S NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL) L2 83 S L1/TI FILE 'USPATFULL' ENTERED AT 15:19:21 ON 08 AUG 2007 L3 2528 S NANOPAR? AND (TAXANE OR PACLITAXEL OR DOCETAXEL OR TAXOL) L426 S L4/AB L5=> s 15 and bioavail? 33602 BIOAVAIL? 14 L5 AND BIOAVAIL? 1.6 => d 1-14 ti ANSWER 1 OF 14 USPATFULL on STN 1.6 TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof

- L6 ANSWER 2 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 3 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 4 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 5 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 6 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 7 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 8 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 9 OF 14 USPATFULL on STN
- TI Novel formulations of pharmacological agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 10 OF 14 USPATFULL on STN
- TI Nanoparticulate delivery systems for treating multi-drug resistance
- L6 ANSWER 11 OF 14 USPATFULL on STN
- TI Nanoparticulate formulations of docetaxel and analogues thereof
- L6 ANSWER 12 OF 14 USPATFULL on STN
- TI Protein stabilized pharmacologically active agents, methods for the preparation thereof and methods for the use thereof
- L6 ANSWER 13 OF 14 USPATFULL on STN
- TI Compositions and methods for administration of pharmacologically active compounds
- L6 ANSWER 14 OF 14 USPATFULL on STN
- TI Protein stabilized pharmacologically active agents, methods for the preparation thereof and methods for the use thereof
- => d 13 ab
- L6 ANSWER 13 OF 14 USPATFULL on STN
- AB In accordance with the present invention, there are provided compositions and methods useful for the in vivo delivery of substantially water insoluble pharmacologically active agents (such as the anticancer drug paclitaxel) in which the pharmacologically active agent is delivered in the form of suspended particles coated with protein (which acts as a stabilizing agent). In particular, protein and pharmacologically active agent in a biocompatible dispersing medium are subjected to high shear, in the absence of any conventional surfactants, and also in the absence of any polymeric core material for the particles. The procedure yields particles with a diameter of less than

about 1 micron. The use of specific composition and preparation conditions (e.g., addition of a polar solvent to the organic phase), and careful election of the proper organic phase and phase fraction, enables the reproducible production of unusually small nanoparticles of less than 200 nm diameter, which can be sterile-filtered. The particulate system produced according to the invention can be converted into a redispersible dry powder comprising nanoparticles of water-insoluble drug coated with a protein, and free protein to which molecules of the pharmacological agent are bound. This results in a unique delivery system, in which part of the pharmacologically active agent is readily bioavailable (in the form of molecules bound to the protein), and part of the agent is present within.

### => d 13 ibib

ANSWER 13 OF 14 USPATFULL on STN

ACCESSION NUMBER:

2003:81474 USPATFULL

TITLE:

Compositions and methods for administration of

pharmacologically active compounds

INVENTOR(S):

Desai, Neil P., Los Angeles, CA, United States

Soon-Shiong, Patrick, Los Angeles, CA, United States American BioScience, Inc., Santa Monica, CA, United

States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: APPLICATION INFO.:

PATENT ASSIGNEE(S):

US 6537579 B1 20030325 US 2000-574763 20000519 (9)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 446783

Continuation-in-part of Ser. No. US 1999-316642, filed on 21 May 1999 Continuation-in-part of Ser. No. US 1998-198082, filed on 23 Nov 1998, now abandoned Division of Ser. No. US 1996-720756, filed on 1 Oct

1996, now patented, Pat. No. US 5916596

Continuation-in-part of Ser. No. US 1995-412726, filed on 29 Mar 1995, now patented, Pat. No. US 5560933

Continuation-in-part of Ser. No. US 1993-23698, filed on 22 Feb 1993, now patented, Pat. No. US 5439686

Continuation-in-part of Ser. No. US 574763 Continuation-in-part of Ser. No. US 1997-926155, filed

on 7 Sep 1997, now patented, Pat. No. US 6096331 Continuation-in-part of Ser. No. US 1994-200235, filed

on 24 Feb 1994, now patented, Pat. No. US 5498421

NUMBER DATE 

PRIORITY INFORMATION:

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LEGAL REPRESENTATIVE:

Pryor, Alton

NUMBER OF CLAIMS:

Reiter, Stephen E., Foley & Lardner

EXEMPLARY CLAIM:

53 1

NUMBER OF DRAWINGS:

0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT:

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